PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
1784wo		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CZ2004/000086	15.12.2004	15.12.2003

International Patent Classification (IPC) or national classification and IPC
A61K35/78

Applicant
PARENTERAL, A.S. et al.

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 6 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
29.06.2005	25.11.2005

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/CZ2004/000086

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1, 2, 6-11	as originally filed
3-5, 5a	received on 17.10.2005 with letter of 15.10.2005

Claims, Numbers

1-6	received on 17.10.2005 with letter of 15.10.2005

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-6
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-6
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-6
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:
   D1: DE 100 41 700 A1 (WIEST, MATHILDE) 14 March 2002 (2002-03-14)
   D2: DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; May 2003 (2003-05), PARKER T D ET AL: "Fatty acid composition and oxidative stability of cold-pressed edible seed oils." XP002320437 Database accession no. PREV200300341311
   D3: WO 95/31176 A (ALMA ROSA, N.V; FIRMA, PETER, RAUSCH; WATSON, DAVID; RAUSCH, PETER) 23 November 1995 (1995-11-23)
   D4: US-B1-6 307 077 (QUEAR ROBERT MICHAEL) 23 October 2001 (2001-10-23)
   D5: SPEISER K ET AL: "HEMP SEED OIL THE WONDER OIL OF THE NEW MILLENNIUM" HAPPI HOUSEHOLD AND PERSONAL PRODUCTS INDUSTRY, DORLAND PUBLISHING, DENVILLE, NJ, US, vol. 36, no. 6, June 1999 (1999-06), pages 106-109, XP000829895 ISSN: 0090-8878

Novelty

2. Claims 1-6 meet the requirements of Art. 33(2) for the reasons set out below..

2.1 None of the prior art documents cited in the search report discloses the production of hemp seed oil by pressurised carbon dioxide extraction. Thus the subject matter of **independent claim 3** and its dependent **claims 4-5 is new** over the cited prior art.

2.1 The **independent claim 1** is directed to "*hemp seed oil obtained by means of carbon dioxide extraction*".

2.1_1 Hemp seed oil, obtained by cold-pressing, is an already known product (see e.g. D1 to D4 below).

D1 (see e.g. claims 1-5 and 8) discloses a dermatological composition for different uses, said composition comprising cold-pressed hemp seed oil as such or in form of an emulsion.

D2 (see e.g. p.733, c.2, l.5-15) discloses the fatty acid composition and antioxidant

stability of several commercially available of cold-pressed edible oils, including that of hemp seed oil.

D3 (see e.g. claims 1-2) discloses a cosmetic nutritive composition comprising cold-pressed hemp seed oil. It also mentions the known availability of edible hemp seed oil (see p.1, §4).

D4 (see e.g. claims 1-2 and 11-12) discloses a method for further purifying crude vegetal oils obtained by cold-pressing, so as to obtain clarified vegetal oils, including hemp seed oil.

2.2$_2$ In the letter of 15.10.05, the applicant states that "hemp seed oil obtained by carbon dioxide extraction" differs from "hemp seed oil obtained by conventional cold-pressing" in that

(i) it is able to bind a broader spectrum of bioactive substances, such as cytokines, CD monoclonal antibodies, arachic acid derivatives, low-molecular peptides or modern antibiotics, and to penetrate and convey them into the deeper skin layers without the use of any synthetic carriers;

(ii) it is stable for a period of at least two years without the necessity to apply any chemical substances; and

(iii) when combined with crude oil, animal or other vegetal bases, it does not loose its efficiency and retains the characteristics mentioned above.

2.2$_3$ Thus, the subject matter of **claim 1** and its dependent **claim 2**, which relate to hemp seed oil obtained by carbon dioxide extraction (i.e. a product *per se*) **is** considered to be **new** over known hemp seed oil obtained by cold-pressing.

2.3 **Claim 6** is directed to the use of the aforementioned "hemp seed oil obtained by carbon dioxide extraction" in pharmaceutical or cosmetic skin preparations. The subject matter of said claims **is** hence also **new**.

Inventive step:

3. Claims 1-6 also meet the requirements of Art. 33(3) PCT for the following reasons:

3.1 The **problem posed** in the present application (see p.3, §2) was to provide means effective as 'conveyor and absorbent agent' (i.e. as penetration enhancer), which

further have the capacity to bind bioactive substances and facilitate their penetration into deeper skin layers without the use of synthetic carriers.

3.2 As proposed in the claims said problem is solved with *hemp seed oil obtained by means of carbon dioxide extraction.*

3.3 The use of "(cold-pressed) hemp seed oil" for cosmetic, therapeutic and nutritional purposes has already been disclosed in the state of the art. With this respect see e.g.

> **D1** and **D3** above, which disclose the beneficial use of hemp seed oil for the treatment of several skin disorders and as skin-care composition; or
> **D5** (p.106, c.1, §1 and p.109, c.1-2) which discloses that the well known nutritional and dermatological benefits of hemp seed oil are due to its perfectly balanced content of EFAs (essential fatty acids), which account for the valuable effects of hemp seed oil in nutritive and skin-care compositions (e.g. in anti-aging, dry-skin, sensitive-skin or after-sun compositions) as well as in therapeutic dermatological formulations for the treatment skin disorders (such as atopic eczema, acne or psoriasis).

3.4 However, nothing in D1, D3 and/or D5, alone or in combination with the other documents cited in the search report, teaches or suggests the alleged beneficial use of "hemp seed oil obtained by carbon dioxide extraction" for binding bioactive substances and facilitating their penetration into deeper skin layers without the use of synthetic carriers.

3.5 Thus, the subject matter of **claims 1-6 involves an inventive step** over the cited prior art.

Industrial applicability:

5. **Claims 1-6** satisfy the criterion set forth in Art. 33(4) PCT because their subject matter is **susceptible of industrial application**.

DE 10041700, be used in an emulsion with emulsifier such as Lizitin, for application onto the inflamed portions of skin. But the inflammation healing agent as per Volume DE 10041700 does not have any satisfactory effect and its applicability period/shelf life is short. When used, the preparation presumes a simultaneous application of the adversely acting synthetic stabilizers and emulsifiers. A cosmetic and therapeutic agent, composed of the hemp oil which is relieved of the oxidation-prone additives that are degrading this non-refined hemp oil via a bacterial biodegradation and that are evoking both the chemical and pharmacological instability, is known from the Volume CZ - U1-13335. When improved like this, the hemp oil can better counteract the action of the UV radiation and has an enhanced capacity to bind upon itself other pharmaceutics. Production of the cosmetic and therapeutic agent per Volume CZ - U1-13335 consists of multiple stages, being very demanding in technological terms, and its manufacturing cycle is very long. Removal of the oxidation-prone additives is incomplete.

Document GB 1356749 is known, which discloses a method of producing vegetable fats and oils by extraction with a solvent, therein the fat or oil is removed from the vegetable matter by extraction with supercritical gases, comprising carbone dioxide. The use of carbone dioxide is based on the inactivity of the inert gas in the respect of the taste and health. With the method according to the document GB 1356749 it is possible for the fats or oils to be completely extracted in their natural composition from the vegetable metrial without chemical modification even of the residue. The

document GB 1356749 does not disclose any other quality or feature of the disclosed method. Document DE 3542932 is known, which discloses a method of a soft extraction of crushed up oil seeds with carbone dioxide. The disclosed method is used due to time efficiency and gentleness in respect to the oil seeds. The document DE 3542932 does not disclose any other quality or feature of the disclosed method.

Object of the invention is to avoid the disadvantages of the state of the art as mentioned above and to provide a natural, more efficient active substance conveyor and absorbent, possessing moreover a better capacity to bind upon itself the bioactive substances, to penetrate into the deeper skin layers, and to convey the bioactive substances without the use of any synthetic carriers, featuring a longer utility period without the necessity to use any conservation chemicals, which - in its primary composition - would also show - without any additives - healing and relaxing effects, preferably in case of the dermal diseases and also contain - in its primary composition - a natural UV protective factor.

Furthermore, the objective of the invention is to provide the method of production of hemp seed oil which - in respect to the state of the art as mentioned above - would better penetrate and convey the active substances into the deeper skin layers without the use of any synthetic carriers and would bind upon itself a broader spectrum of the bioactive aubstances. A further objective is to produce an agent which with these properties easily and reliably in the industrial conditions.

Subject-matter of the Invention

To a major extent the disadvantages of the current state of technology are eliminated and the invention objectives achieved by a hemp seed oil for transfer and absorption of active substances of pharmaceutical and cosmetic preparations into the skin according to the invention consisting in that it is a product of extraction of the milled down hemp seeds by means of carbon dioxide. Advantageously one weight share of the extract may create a mixture with two weight shares of the solution containing up to 30 % in weight of sodium bicarbonate. The invention objectives are also achiebed by a method of production of hemp seed oil for transfer and absorption of active substances of pharmaceutical and cosmetic preparations into the skin, consiting in that the hemp seeds are milled down to hemp flour, then pressure-extracted by means of the carbon dioxide to hemp oil. Advantageously, hemp seeds may be milled down to a fine hemp flour, the milled down hemp flour then poured into the extraction cartridges that are then inserted into the extractor; the extractor gets closed and carbon dioxide is driven into it at the temperature between about 35 °C - 45 °C and under pressure between 25 MPa - 35 MPa, advantageously at 40 °C and the pressure 20 Mpa, with the hemp oil extraction process slowed down the carbon dioxide pressure in the extractor is reduced down to the value of the ambient atmospheric pressure and the hemp oil is separated from the carbon dioxide, then the carbon dioxide is taken out of the extractor to a reserve tank and stored there in its supercritical condition. Advantageously, 2 % - 35 % in weight of the crushed silicon sand may be mixed into the

extracted hemp oil for removal of the chlorophyll and waxes; following the surface absorption, the crushed silicon sand is filtered out. According to the invention the hamp seed oil manufactured by a method according to the invented method of production may be used for transfer and absorption of active substances of pharmaceutical and cosmetic preparations into the skin.

The cosmetic, dietetic, and therapeutic preparations containing a conveying and absorption agent for conveying the active substances according to the invention have better efficiency as the conveying and absorption agent has a strong capacity to bind upon itself the bioactive substances. Unlike the agents known until now, the conveying and absorption agent according to the invention is able to bind upon itself a broader spectrum of the bioactive substances such as e.g. cytokines, CD monoclonal antibodies, arachid acid derivates, low-molecular peptides, modern antibiotics, and other substances, to penetrate and convey them into the deeper skin layers without the use of any synthetic carriers. The conveying and absorption agent according to the invention does not irritate skin, but on the contrary has more bio-chemical qualities, is healing eczema, acne, and relaxes notably psoriasis without application of any other active substances

Patent claims

1. Hemp seed oil for transfer and absorption of active substances of pharmaceutical and cosmetic preparations into the skin,
c h a r a c t e r i s e d b y t h a t
it is a product of extraction of the milled down hemp seeds by means of carbon dioxide.

2. Hemp seed oil according to the claim 1,
c h a r a c t e r i s e d b y t h a t
one weight share of the extract creates a mixture with two weight shares of the solution containing up to 30 % in weight of sodium bicarbonate.

3. A method of production of hemp seed oil for transfer and absorption of active substances of pharmaceutical and cosmetic preparations into the skin,
c h a r a c t e r i s e d b y t h a t
the hemp seeds are milled down to hemp flour, then pressure-extracted by means of the carbon dioxide to hemp oil.

4. A method of production according to the claim 3,
c h a r a c t e r i s e d b y t h a t
hemp seeds are milled down to a fine hemp flour, the milled down hemp flour is then poured into the extraction cartridges that are then inserted into the extractor; the extractor gets closed and carbon dioxide is driven into it at the temperature between about 35 °C - 45 °C and under pressure between 25 MPa

- 35 MPa, advantageously at 40 °C and the pressure 20 Mpa, with the hemp oil extraction process slowed down the carbon dioxide pressure in the extractor is reduced down to the value of the ambient atmospheric pressure and the hemp oil is separated from the carbon dioxide, then the carbon dioxide is taken out of the extractor to a reserve tank and stored there in its supercritical condition.

5. A method of production according to the claim 3 or 4, c h a r a c t e r i s e d b y t h a t 2 % - 35 % in weight of the crushed silicon sand is mixed into the extracted hemp oil for removal of the chlorophyll and waxes; following the surface absorption, the crushed silicon sand is filtered out.

6. A use of the hamp seed oil manufactured by a method according to one of the claims 3-5 for transfer and absorption of active substances of pharmaceutical and cosmetic preparations into the skin.